

chain nodes :

12 13 14 15 16 17 18 19 20 21 22 24

ring nodes :

1 2 3 4 5 6 7 8 9 10 11

chain bonds :

2-6 2-22 3-13 3-14 4-15 4-20 5-16 5-21 7-19 8-18 9-24 11-12 16-17

ring bonds :

1-2 1-5 2-3 3-4 4-5 6-7 6-11 7-8 8-9 9-10 10-11

exact/norm bonds :

1-2 1-5 2-3 2-6 3-4 4-5 4-15 6-7 6-11 7-8 8-9 9-10 9-24 10-11 11-12

exact bonds :

2-22 3-13 3-14 4-20 5-16 5-21 7-19 8-18 16-17

G1:0,NH

Match level:

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:CLAS513:CLAS514:CLASS 15:CLAS516:CLAS517:CLAS518:CLAS519:CLAS520:CLAS521:CLAS522:CLAS524:CLAS5

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                 MEDLIRE segment
                 MEDLINE and LMEDLINE updated with 2008 MeSE vocabulary
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- ANSWER 1 OF 10 CARLOS CORYRIGHT 2007 ACS ON STO 3.4
- $\Delta N_i$ 2007: 1323735 CAPLOS

147:461654 ÐQ

- Characterization of the Metabolic Activation of Repatitis C Virus 27.25 Eucleoside Inhibitor B-D-2'-Deoxy-2'-fluoro-2'-C-methylogiidine (PET-4030) and Identification of a Bovel Sorive 5'-Triphosphate Species
- Ma, Man; Siang, Wen-Wong; Bobledo, Micole: Leveque, Vincent; Bli. Semir; Lara-Jaiwe, Terese; Masjedizadeh, Mohammad: Smith, David S.: Commack, Nick; Klumpp, Blass; Symons, Julias Rooms Palo Alto LLC, Palo Alto, CA, 94304, USA
- 08
- 5975 Journal of Biological Chemistry (2007), 282(41), 29812-29820 COCKU: JBCBA3; IŠSN: 9021-9258
- American Society for Biochemistry and Molecular Biology 933
- $\Sigma \Sigma \Sigma$ Journal
- ĿΑ English
- Rupu2: beoxy-2: "fluoro-2: "C-wethylovtidise (F61-61:0) is a potest AB ishibitor of hepatitis C virus (MCV) replication is the subgenemic SCV replicon system, and its corresponding 5' -triphosphate is a potent inhibitor of the SCV PNS polymerase in vitro. In this study the formation of PSI-5130-triphosphete was characterized in primary human bepatocytes. PSI-6130 and its 5'-phosphorylated derivs, were identified, and the incracellular conons, were determined. In addition, the desminated derivative of PSI-ELEO, B-0-2'-deoxy-2'-Elsoro-2'-C-methyluridine (RO2403, PSI-6026; and its corresponding pheaphorylated metabolites were identified in human hepathoytes after incubation with DSI-6130. The formation of the 5'-triphosphate (TF) of PSI-6130 (PSI-6130-TF) and PO2433 (RO2433-TF) ingreased with time and reached stoady state levels at 48 h. The tormation of both PSI-6130-TP and RO2413-TF demonstrated a linear relationship with the extracellular comms, of PSI-6130 up to 180 pm. suggesting a high capacity of human hapatocytes to generate the two triphosphates. The mean half-lives of FST-6130-TP and RC2433-TP were 4.7 and 38 b, resp. 802433-TP also inhibited ENA synthesis by the bative SCV replicase isolated from BCV repliced calls and the received excellent polymerase WSSB with potencies comparable with those of FSY-6130-TP. innorporation of XO2413-5 -monopresphate (MP) into hawcast ANA by N858 led to chain termination similar to that of PSI-6130-MF. These results demoinstrate that F31-6130 is metabolized to two pharmacol. active species in primary homes bepatocytes.
- 817204-44-7, 931-8130-tripbosphate Ph: 88) (Biological study, unclassified;; PAC (Pharmscological activity); FRY (Pharmscokinetics): THU (Therapeutic use): BIOL (Biological study): USSS (Uses)
  - (characterization of metabolic activation of hepatitis C virus sucleoside inhibitor \$-6-2'-deoxy-2'-flworo-2'-C-methyloytidine (MER-C130) and identification of a novel active 5 -- triphosphate 39903833
- \$17284-44-7 CAPACE EN
- Cyclaine 51-(betrabydrogen briphosphate). 21-deoxy-21-fluoro-21-methyl-. (2:R)~ (CB IGDEX NAME)

Absolute stereochemistry.

37 817264-33-4, \$61-6330

RL: DWA (Drug mechasism of action); PAC (Pharmacological activity); PXT (Pharmacokinetics); THV (Therapeutic use); BIOL (Biological study); UBEB (Uses)

(characterization of metabolic activation of hepatitis C yirgs nucleoside inhibitor  $\beta$ -D-2'-deoxy-2'-fluoro-2'-C-methyloytidine (PSI-6)30) and identification of a novel active 5'-triphosphate species)

RM 817204-33-4 CAPLUS

CR Cytiding, 2"-deczy-2"-fluoro-2"-methyl-, (2"R)- (C8 limber Name)

Absolute stereochemistry. Notation (+).

RE.CRT 25 THERE ARE 25 CITED REPRESCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE POPMAT

54 AMENER 2 OF 10 CAPIA/S CONTRIGHT 2007 NCS on SEC

AN 2807:877688 CAPLUS

DD 147:39788)

Ti Sharmookinstics of the autiviral agent 8-D-2'-deaxy-2'-fluoro-2'-Cwethyloytidine in rhesus monkeys

BU Asif, Chazia: Burwitz, Selwyn J.; Shl. Jusxing: Bernander-Santiago, Brenda 1.; Schinezi, Raymond P.

CB Department of Pediatrios, Emory University, Stiants, GA, 30322, MSA

80 Antimicrobial agents and Chemotherapy (2007), 51(8), 2877-2882 CODED: AMACCQ: ISSN: 0056-4804

PB American Bodiety for Microbiology

Pf Journal

dalipe% Ad

B-D-2'-Deoxy-2'-fluoro-l'-C-methylcytidine (%81-6130) is an effective AB. ishibitor of hepatitie C virus (807) replication is vitro. The purpose of this study was to evaluate the single-dose pharmacobisetics of FS:-6130 in rnesus monkeys following i.v. and oral administration. Noncompaxtmental anal, of the serum data obtained following oral and i.v. administration was performed. Tharmscokinetic studies with rhesus monkeys indicated slow and incomplete absorption with a mean absorption time (MAT) of 4.6 h and an oral bloavailability of 24.0% x 14.3% (mean x standard deviation), with comparable mean apparent half-lives following i.v. (4.50 t 1.98 b) and oral (5.64 t 1.13 b) administrations. The sverage percentages of the tetal dose recovered unchanged and in decalinated form in the urite were 32,9% ± 32.6% and 38.9% ± 6.6% (2.0.) and 6.0% ± 3.9% and 3.9% it [ 08 (oral), resp. The total bloavallability, taking into second the parent drug and its deaminated metabolite 2'-deoxy-2'-floare-2'-Cmethyluridise (PSE-6206), was 44% i 26%. PSI-6130 was present in the cerebrospical field after oral and i.v. dosing. However, no desmination of radiolabeled PSI-4)38 was detected after 8 h of incubation in monkey and human whole blood. An W4-modified prodrug of FSI-6130 (PSI-6419) was orally administered to wonkeys, but it failed to improve the oral bicavailability of PSE-6138. Further studies are warranted to improve the oral bicavailability and reduce the deamination of PSI-6130 in order to

explore the potential of this drug for the treatment of  $\mathtt{MOV-infected}$  is dividuals.

19 863329-66-2

- KL( BSO (Biological abudy, unclassified); BDDL (Biological study) (PSI-6206; pharmacokinatics of antiviral deoxyfluoromethyloytidine in theses monteys)

RM 863029-66-2 CAPLOS

CR Uniding, 21-decay-21-fluoro-21-methyl-, (218)- (201) (CA IGDEN NAME)

absolute stereocsemistry. Botation (\*).

TT 950323~07~5F

RL: FET (Phermacobinetics): SEN (Synthetic preparation); THO (Therepeutic use): BIOL (Biological study): PREF (Preparation); VSES (Mass)

(\$61-6419; pharmacokinetics of antiviral decryfinoromethylcytidias in theses monkeys)

PR 950923-07-6 CAPEGS

CM - ERDEY NAME DOT YET ASSIGNED

absolute stereochemistry.

TT 837204-33-4, PS3-6130

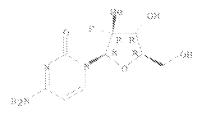
EL: PXT (Pharmsockinetics); TBU (Therapeutic see); E105 (Biologics) study); USES (Gses)

- (pharmacckinetics of antivira) decryflocromethylcytidine in rhescs - workers)

%n 8)7204-33-4 CAPLOS

CN Cycldine, 2'-deoxy-2'-flaoro-2'-methyl-, (2'%)- (C% IGDEN NAME)

Sbsolute stereochemistry. Botation (+).



RE.ONT 23 THERE BUE 23 CITED BEFERENCES AVAILABLE FOR THIS MECOND ALL CITETIONS AVAILABLE IN THE RE FORMAT

LA AMENER 3 OF 10 CAPGGS COPYRIGHT 2007 ACE ON STY

AN 2007:640930 CMFUUS

98 JA7:53103

Freparation of adylated (2°F)-2'-deoxy-2'-fluoro-2'-methyloytidines as antiviral agents

18 Chun, Byoung-Ewon; Clark, Jerewy; Barma, Keehab; Mang, Pelyuan

PA F. Boffmann-La Roche A.-G., Ewitz.; Pharmseset Inc.

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SU FOT Lat. Appl.: 44pp.
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		CBL CB,	ČR.,	$CW_{i}$	C&,	DX.,	DX,	DM,	DI.	BC,	BE.	BG,	88,	₩X,	98,	36,
		021, 681,	13.83	$\mathcal{C}_{X,X}^{\alpha,\alpha,\alpha}$	3007	3887	380 /	ED,	3.33.3	IN,	13,	J₽,	8.8	879	8287	EN.
		KP, KR.	82.	ĐA,	LC.	ъж,	ESE,	Σξ.,	ΣX.	X.8 ,	Х.У.,	2.2.	May,	MO,	MO,	ME.
		BA, MW,	MX,	$NN_{\rm c}$	$MZ_{\mathcal{F}}$	NS.	WG.	QX,	QO,	82.	OM.	PVJ.	PS.	PL	$p_T$	80,
		887 897	80.	800,	SE,	SG,	ЗЖ,	38.	38.85	39,	87,	vJ,	TM,	TH,	TE,	$m_{\Sigma}$
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- as Acylated suchosides I (R) = aikyl, alkony) and their salts, useful as antimizal agents, are prepared by adylation of I (R) = R). Formulations containing I (R) = i-PrO; were given.
- IT 940908-81-67
  Rb: PAC (Pharmacological ectivity); %CT (Rescussi); SFB (Synthetic preparation); TBO (Thermpentic use); SIGE (Biological study); SFEP (Preparation); RACT (Rescusst on reagent); VSES (Vses) (preparation of sayisted (2/8)-2'-deoxy-2'-fluoro-2'-methylogicalines as antiviral agents)
- BN 940908-81-6 CARLUS
- CE Cytisise, 2'-decxy-2'-fluoro-1'-wethyl-, 3',5'-bis(propyl carbonete), (2'R)- (CE IGDEX NAME)

Absolute stereochemistry.

17 940908-78-18 940908-79-28 940908-80-58
940908-82-78

EL: PAC (Frankschiogical scrivity); SFS (Symbatic preparation); TSD (Therapeutic osa); STOL (Biological study); PREF (Preparation); DSBS

Absolute stereochemistry.

RE 940908-79-2 CAPLOS CN Oytidine, 2'-deoxy-2'-fluoro-2'-methyl-, 3',5'-bis(2-methylpropaposts), (2'R)- (CB IGDEX NAME)

Absolute stereochemistry.

BM 940008-80-5 CARLOS CB Cytidise, 2'-decxy-2'-fluoro-2'-methyl-, l',5'-bis(2-methylpropyl carbonate), (2'%)- (CA IBDEX NAME)

Absolute stereochemistry.

Apsolute stereochemistry.

**- (8**8 - 1893).

11 817204-33-4

RM 817204-33-4 CAPEDS

CW Cytidine, 2'-deoxy-2'-figoro-2'-methyl-, (2'8)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

BRIGHT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS PRESPO ALL CITATIONS SYSTEADLE IN THE RE FORMAT

14 SHOWER 4 OF 10 CAPLUS COPYRIOWS 2007 ACE OF STN

59 2007:147988 CAPLOS

DB 1450397253

TI Mechanism of activation of β-D-2'-deoxy-2'-fluoro-2'-C-methyloytidine and inhibition of hepatitis C virus NSSS NNA polymerase

BU Marakami, Bisuke; Beo, Balying; Remesh, Mangele; McGrayer, Tamera F.; Whitaker, Tony; Micolocnick Steuer, Holly M.; Schinezi, Raymond F.; Stoyver, Lieven J.; Obikhod, Bleksandr; Otto, Michael J.; Furman, Phillip

CB Pharmasset, Inc., Princeton, NJ, 68546, BSA

BG Astimicrobial Agents and Chemotherapy (2007), 51(2), 503-509 CODEN; AMACCQ: IBSN: 6066-4804

FS American Society for Microbiology

DY Journal

ia English

6-6-27-Deoxy-27-Eleore-27-C-methylogidine (PSI-613C) is a potent 38.83 specific inhibator of hepatitie C virus (MCV) RBA synthesis in Bub-7 replicos celis. To imbibit the HCV MS98 RNA polymerase, FSI-6130 must be prosphoryisted to the 5'-triphosphate form. The phosphorylatios of FBT-6130 and inhibition of BCV MSSS were investigated. The phosphoryisticm of P81-6130 by recombinant human 2'-decayoycidine kinase (dCX) and uriding-cytiding kinase 1 (VCX-1) was measured by using a coupled spectrophotometric reaction. Y81-8130 was shown to be a substrate for purified dCF, with a Nut of 81 µM and a koat of 0.007 s-1, but was not a substrate for VCX-1. FS1-6130 monophosphete (PS1-6130-MP) was efficiently phosphorylated to the diphosphate and subsequently to the triphosphate by recombinant human DMP-CMP kinase and auclioside diphosphate kieses, resp. The inbibition of wild-type and mutated (SZ8ZT) BCV NSSB RNs polymerases was studied. The steady-state inhibition constant [F1] for PSI-6130 triphosphate (PSI-6130-TP) with the wild-type enzyme was 4.3 µR. Similar results were obtained with 2'-C-methyladenosine triphosphace (Xi = 1.5 kM) and 2'-C-methylcytidine triphosphate (Xi = 1.6 pm). 035% with the SZ8ZF mutation, which is known to confer resistance to Z:-C-methyladenosine, was inhibited by FEI-6136-7% as efficiently as the wild-type. Incorporation of PSI-6136-MP into EN&

Absolute Stereochemistry.

BX 932721-63-6 CARLUS CB 5'-Cytidylic soid, 2'-dsoxy-2'-flsoro-2'-methyi-, (2'8)- (CA IGDEX MAKE)

Absolute Stereochemistry.

Absolute starsochemistry.

TT 817204-33-4, ESI 6130
Pt. BED (Siological study, pacissified); PRP (Properties); BIGE (Biological study) (mechanism of scrivation of \$-0-2'-deoxy-2'-fluoro-2'-C-methylighted and inhibition of hepatitin C virus NSSB ENA polymerase; B17204-33-4 CAPLUB
CC Cytidise, 2'-deoxy-2'-fluoro-2'-methyl-, (2'R)- (CA INDEX NAME)

Absolute stereochemistry. Botation (4).

dsodellom

HELICHT 29 THERE ARE 29 CITED REPERENCES AVAILABLE FOR THIS RECORD ARC CITATIONS AVAILABLE IN THE RE PORMAT

- IA AMSWER 5 OF 10 CAPIAS COFFRIGHT 2007 ACS ON STR
- AN 2008:988353 CAPLUS
- DB 145:505687
- TI Synthesis of 2-deoxy-2-fluoro-2-6-wethyl-6-ribofurancese
- AU Clark, Jeremy L.; Mason, J. Christian; Bobbs, Asm J.; Hollacker, Laurent; Schinazi, Raymond P.
- C8 Pharmasset, lac., Tecker, GB, VBA
- 30 Journal of Carbohydrate Chemistry (2008), 25(6), 481-470 CODEM: JCACOM: ISSN: 0732-8303
- PS Taylor & Francis, Inc.
- Of Journal
- La Esglish
- OS CASERACT 148/505687
- AB The synthesis of Me 3.2-di-O-bentoyl-2-deoxy-2-fluoro-2-C-methyl-B-D-ribofurenoside and the conversion to the corresponding i-O-acetyl-3.5-di-O-benzoyl-2-deoxy-2-fluoro-2-C-methyl-D-ribofurenose and 1.3.5-tri-O-benzoyl-2-deoxy-2-fluoro-2-C-methyl-D-ribofurenose is reported. The key synthetic step is the fluorisation of the tertiary center of Me 3.5-di-O-benzyl-2-C-methyl-B-D-arabinofurenoside to growide Me 3.5-di-O-benzyl-2-deoxy-2-fluoro-2-C-methyl-B-D-ribofurenoside.
- TF 817204-32-3P 874636-94-5P
  - BL: GPD (Synthetic preparation); PRBP (Preparation) (synthesis of 2-deoxy-2-fluoro-2-C-mathyl-G-ribofbrancess yis fluorination of the terriary center of Me 3,5-di-O-benzyl-2-G-mathyl-G-D-arabinoforanceides)
- AB 817204-32-3 CAPLUS
- CN Cyciding, W-benzoyi-2'-deoxy-2'-fluoro-2'-methyl-, 3',5'-dibenzoste, (2'x)- (2C1) (CA INDEX MAMB)

Absolute stereochemistry. Rotation (\*).

- RM 874638-84-5 CAPLUS
- CN Benramide, N-|1-{(28)-3,5-di-O-benroyl-2-deoxy-2-fluoro-2-methyl-u-berythro-pentofurasosyl}-1,2-dibydro-2-oxo-4-pyrimidinyl|- (9CI) (CA INDEX 8ASE)

Absolupe spereochemistry.

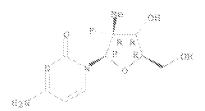
EB.OGT 26 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

- (4 BERRER 6 OF 10 CREECS COPYRIGHT 2007 ACS OF SYN
- 89 2006:478128 CAFLUS

#### 10/838,793

- DG 145:202057
- Inhibition of hepatitis C replicon ANA synthesis by 6-0-2'-deoxy-2'-Charro-2'-O-wethyloytidise: a specific inhibitor of hepatitis C virus replication
- AB Stuyver, Lieves J.; McDrayer, Tamara P.; Tharmish, Phillip M.; Clark, Jerusy; Hollecker, Laurest; Lostia, Stefania; Nachman, Taumy; Grier, Jason; Sensett, Matthew A.; Rie, Weng-Yu; Schinszi, Raymond P.; Morrey, Sone D.: Julander, Sustia L.: Furman, Phillip A.: Otto, Michael J.
- C3 Pharmasset Inc. Princeton, NJ, USA
- Artiviral Chemistry & Chemotherapy (2006), 17(2), 79-87 30 CODEN: ACCRESC; ISBN: 0956-3262
- 28 International Medical Press, Ltd.
- 8FF Boornall.
- English X.A
- B-D-2:-Decay-2:-fluoro-2:-C-wethyloytidine (PSI-4130) is a cytidine 5.38 analog with potent and selective anti-bepatitis C virus (BCV) activity in the subgenomic BCV replicon assay, 90% effective concentration (EC90) - 4.6 f. 2.0 pM. The spectrum of activity and cytotoxicity profile of Pg1.6136 was evaluated against a diverse panel of viruses and cell types, and against two addel. BCV-ib replicoss. The 8282T mutation, which confers resistance to 21-C-Me adenosine and other 21-methylated modleosides, showed only a 6.5-fold increase in EC90. When assayed for activity against bovine diarrhoes virus (8909), which is typically used as a surrogate assay to identify compds, active against BCV, PSI-6130 aboved so apti-2909 activity. Weak antivital activity was noted against other flavininuses, isoluding West Wile virus, Gengus type 2, and yellow fever virus. These results indicate that FSI-6130 is a specific immigitor of MCV. F31-6130 showed little or so cytotoxicity against various cell types, including human peripheral blood mononuclear and human bone marrow progenitor cells. We mitochemitial texicity was observed with PEI-5130. reduced activity against the RdRp 81817 mutant suggests that \$31-6130 is an inhibitor of replicon BNS synthesis. Finally, the no-effect does for mice treated i.p. with YSL-6130 for six consecutive days was 2100 mg/kg per day.
- 817204-33-4, PSY 6130 Pin ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THE (Therapentic use); BIOL (Biological study); OSBS (Oses)
- (PSI-6130 inhibition of begatitis C replicon RNA synthesis)
- 817204-33-4 CAPINS
- Cytidise, 2'-deoxy-2'-fluoro-2'-methyl-, (2'8)- (CA INCEX MANE) CD.

Absolute starsochemistry. Rotation (\*).



EE.CEE 36 THERE ARE IS CITED REFERENCES SYSTLABLE FOR THIS PROOPE ALL CITATIONS AVAILABLE IN THE RE FORMAT

- AGSWEE 7 OF 15 CAPLUS COPYFIGHE 2007 ACS on SER 1.3
- 2006:269477 CAPLUS AΩ
- 146:012289 83N
- 113 Preparation of slkyl-substituted Z-deoxy-Z-fluoro-D-xibofuranosyl pyrimidine and purine medieoside analogs via condessation of the lactone to nucleosides as potential sativiral agents
- Chun, Byonsg-Kwon; Wang, Pelysan 1.10
- PΑ Pharmasset, Inc., 898
- PCT Int. Appl., 74 pp. 80
- COORDAY BIXXD2
- $\Omega$ Patest
- E.A. Raglish
- FAG. CNT 3

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CW, CO, CB, CD, CZ, GB, GF, GM, GZ, EC, EE, EG, ES, FI, GR, GD,
             CE, GE, GM, BE, BU, IO, IE, IN, IS, JP, KE, NG, NM, NP, NE, NY,
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            KR, KK, KW
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             ES, ET, DT, DB, EV, MC, ND, PD, PT, NO, SB, SI, SE, TB, MF, MB,
             CY, CG, CI, CM, CB, CM, CQ, GW, SE, SM, CE, SN, MO, MG, SW, GM,
             GM. KM. LS. WW. MK. MA. SG. SL. SK. TK. GG. SM. SM. AM. AM. MK.
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                                           WS 2005-225425
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     EP 1889303
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                               20070725
                                           EP 2005-808357
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        P: BT, BE, BG, CB, CY, CZ, GB, GN, EE, BS, PI, FR, GB, GR, BV, IX, ES, IT, LI, LT, LU, LV, BC, NL, PL, BT, RO, EE, SY, SE, TE, AL,
             BA, RE, ME, YD
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                                            IN 2007-EW1283
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     FX 2007093393
                                20070938
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     WO 2005-0332406
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    MARRET 144:312289
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\* STEUCTURE DIAGRAM TOO LARGE FOR DISPLAY -- AVAILABLE VIA OPPLINE EPINT \*

A process for preparing of 2-deoxy-2-fluoro-2-methyi-D-ribosolactomes, I. whereis R1 and P7 can independently be M, CH3, acetyl, benzoyl, pivaloyl, 4-mitrobenzoyl, 3-mitrobenzoyl, 2-mitrobenzoyl, 4-chlorobenzoyl, 3-chlorobenzoyl, 2-chlorobenzoyl, 4-methylbenzoyl, 3-methylbenzoyl, Z-methylbenzoyi, 4-phecylbenzoyi, benzyl, 4-methoxybenzyl, trityl, trialkyisilyl, t-butyl-disikyläilyl, t-butyldiphenyisilyl, TIPDS, TRP, MOM, or MES are prepared and used is the condensation to 2-decay-2-fluoro-D-ribofuranosyl pyrimidina and purine nucleoside analogs. Thus, 2-decxy-1-fluoro-D-ribofbrehosyl pyrimidine and purise hacleoside analogs II and III, whereis X is a halogen; Y is N or CH; E is a halogen, bycroxyl, ether, thick thicether, (un) substituted amine or mixyl) R1 is alkyl, vinyl, ethycyl: R2 and R3 cas be some or different B, mikyl, anylalkyl, acyl, byclic acetal such as 2',3'-0-isopropylidene or 21,3-0-benzylidene, or 21,31-cyclic carbonate; R4, R5, and R5 are independently 8, halogen, bydroxyl, ather, thiol, thicether, N3, (un)aubstituted amine, (un)substituted amido, alkyi, halogenated alkyi, alkeny), halogenated alkenyl, alkynyl, halogesated alkynyl, hydroxy alkyl, alkony are prepared and are potential auti-600 agents. Epecifically, IV was propared in 38 % yield via condensation, slkylation and stereoselective Phorisation resolions and can exhibit potential use as an enti-sery egest. 879581-07-28

RD: FMF (Industrial manufacture); SPN (Synthetic preparation); FRSP (Fremaration)

(preparation of alkyl-substituted 2-deoxy-2-fluoro-D-ribofurenosyl pyrimidine and period nucleoside analogs via condessation of the lactone to suckeosides)

RM 87055%-07-2 CAPEMS

CR Cytidine, N-benzoyl-2'-denxy-2'-fluoro-2'-wethyl-, 3',5'-bis(2,2-dimethylpropanoste), (2'R)- (90X) (CA INDER NAME)

Spsolute stereochemistry.

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ANSWER 8 OF 10 CAPLOS COPYRIGHT 2007 ACS OR STE
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 $\lambda \delta$ 2006:103884 CAPLOS

983 144:171198

323 Preparation of alkyl-substituted Z-deoxy-Z-fluoro-b-ribofurancay). pyrimiding and purine accleosade analogs via congensation of the lactors co nocleosides as potential activital agests

Mang, Pelyman, Stec, Wojclech; Clark, Jeremy; Chun, Mynung-Kwon; Shi, 3.3Sunking: Du. Jiefs Pharmasset, Inc., DSA

 $\Sigma \Delta$ 

 $\{0,0\}$ ECT Int. Appl., 34 pp. CODER: PIKRD2

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81	WO	) 2006012440 ) 2006012440			8.8		20060202											
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# \* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIE OFFLIRE PRINT \*

A process for preparing of 1-deoxy-2-fluoro-1-methyl-0-mibonolactones, I, wherein Pl and R2 can independently be W. CB3, acetyl, behroyl, piwaloyl, 4-mitrobeanoyi, 3-mitrobenzoyi, 2-mitrobenzoyi, 4-chicrobenzoyi, 3-chlorobeszoyl, 2-chlorobeszoyl, 4-methylbenzoyl, 3-methylbenzoyl, 2-methylbenzoyl, 6-phenylbenzoyl, benzyl, 6-methozybeszyl, trityl, trialkylsilyl, t-butyl-dialsylsilyl, t-butyldiphenylsilyl, TIPDS, TEP, MOM, or MSN are prepared and used in the condensation to 2-decay-2-fiboro-D-ribofuranosyl pyrimidine and purine muchecise analogs. Thus, 2-deoxy-2-fluoro-D-ribofnranosyl pyrimidine and purise nucleoside analogs II and III, wherein X is a balogen; Y is B or CB; I is a belogen,

bydroxyl, ether, thiol, chicether, (un)substituted amine or alkyl, %1' is alkyl, vinyl, ethynyl; %2' and %3' can be same or different B, alkyl, arylalkyl, acyl, cyclic acetal such as 2',3'-C-isopropylidene or 2',3'-cyclic carbonate; %4, %3, and %6 are independently M, baloges, hydroxyl, ether, thiol, thioether, nl, (un)substituted amide, alkyl, halogenated alkyl, alkesyl, balogenated alkynyl, hydroxy alkyl, alkoxy are prepared and are potential anti-ECV agests. Specifically, IV was prepared (no yield, claimed) via condensation, alkylation and stereosciective fluorisation reactions and can exhibit potential use as an anti-80V agent.

TY 817204-12-3F 817204-33-4F 874636-62-1F

874638-94-5P 874638-98-98

BL) IMP (Industrial manufacture); SPN (Synthetic preparation); FREP (Preparation)

(preparation of alkyl-substituted 3-deoxy-2-fluoro-D-riboforancey) pyrimiding and purine nucleoside analogs via condensation of the lectons to nucleosides)

BN \$17204-32-3 CAPUUS

CE Cytidine, B-beszoyl-Z'-deoxy-Z'-flaoro-Z'-methyl-, 3°.5'-dibenzoste, (2°8)- (90) (08 INORK BANK)

Absolute stereochemistry. Botation (\*),

N 837264-30-4 CAPEDS

CB Cyvidine, 2'-deoxy-2'-fiboro-2'-methyl-, (2'%)- (CS INDEX BAME)

Absolute stereochemistry. Rotation (+).

EN 874638-82-1 CAPISS

CB Benzamide, R-;i-{(2R)-5-0-benzoyl-2-deoxy-2-flooro-2-methyl-3-0-(methylsulfonyl)-6-0-erythro-pentoforanosyl}-1,2-dihydro-2-ozo-4pyrimidinyl)- (9Cl) (CA INDEX BAME)

Absolute stereochemistry.

XM 874638-94-8 CAPAGS

CN Benzawide, B-(1-|(28)-3.5-di-O-benzoyi-2-deoxy-2-fluoro-2-methyl-q-0erythro-pentofuranczyl]-i,2-dibydro-2-oxo-4-pyrimidinyi}- (901) (CB INDEX Name:

Absolute stereochemistry,

XB 874638-98-9 CAPLOS

CM Cytidine, G-benzoyl-2'-denxy-2'-fluoro-2'-methyl-, (2'E)- (9CI) (CA IMPEX NAME)

Absolute stereochemistry.

- 14 ABSWEE 9 OF 10 CAPLUS COPYRIGHT 2007 ACS On STE
- A8 2005:648160 CAPLUS
- DN 143:248687
- TI Design, Systhesis, and Astiviral Activity of 2'-Deory-2'-fluorout'-C. astbyi-Cytidise, a Forest Labibitor of Mepatitis C Virus Replication
- AU Clark, Jeremy L.; Hollecker, Laurent; Mason, J. Christian; Stayver, Lieyen J.; Tharnish, Phillip M.; Loscia, Stefania; McBrayer, Tamara K.; Schinazi, Paymond K.; Natanabe, Kyoichi A.; Otto, Michael J.; Purman, Phillip A.; Stec, Wojciach J.; Patterson, Steven E.; Pankiewicz, Exzysztof W.
- CB Fharmasset, Inc., Princeton, MJ, 98349, 93A
- SG Journal of Medicinal Chemistry (2005), 48(17), 5504-5568 CODEN: JMCMax: X88%: 0022-2623
- 88 American Chemical Society
- Dr Journal
- Es. Buglish
- 08 CBSPERCY 143:248607
- AB The pyrimidine nucleosise- B-D-2'-deoxy-2'-fluoro-2'-0-methyloytidine
  (I) was designed as a bepatitie C virus RNA-dependent RNA polymerase (NCV PdPp) inhibitor. The title compound was obtained by a DAST fluorination of R4-bestoyl-1-f2-methyl-3,5-di-D-bestoyl-B-D-arabinofurasosyl)cytosine to provide M4-benzoyl-7(2-ficoro-2-methyl-3,5-di-D-bestoyl-B-D-ribofurasosyl)cytosine. The protected 2'-C-methyloytidine was obtained as a byproduct from the ORET fluorisation and allowed for the preparation of two biol, soulve compds. From a common precursor. Compound I and 2'-C-methyloytidine were assayed is a sub-genomic ECV replicon assay system and found to be potent and selective inhibitors of ECV replication. Compd.1 shows increased inhibitory activity is the ECV replican assay compared to 2'-C-methyloytidine and low cellular toxicity.

  IT 817204-13-4F
- AL: PAC (Pharmacological activity); PCT (Reactant); SPN (Synthetic preparation); RIOL (Biological Study); PREP (Preparation); RACT (Reactant
  - or reagent)
    (design, synthesis via fluorination, and antiviral activity of 2'-deoxy-2'-fluoro-2'-C-methyl-cytidine, a potent inhibitor of Sepatitie C virus replication)

817204-33-4 CAPLOS

Cytidine, 2'-deoxy-2'-fluoro-2'-wethyl-, (2'E)- (CA EMBE WAME)

Absolute stereochemistry. Potation (\*).

863339-66-29  $\mathfrak{T}\mathfrak{T}$ 

Pir PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PRER (Preparation)

(design, synthesis via flucrimation, and antiviral activity of 2'-dsoxy-2'-fluoro-2'-C-methyl-cytidise, a potest ishibitor of

Repatitiz C Virus replication)

863329-66-2 Carlus 80

Wriding, 21-deoxy-21-Elepro-21-methyl-, (218)- (901) (de INOEX RAME)  $\mathbb{C}\mathbb{N}$ 

Absolute stereochemistry. Rotation (\*).

817204-32-38 860329-85-18

Bir PCT (Reactabl); SPN (Syothetic preparation); PRSP (Preparation); PACT (Peactast or rasgest)

(design, synthesis via fluorination, and antiviral activity of 2'-deoxy-2'-fluoro-2'-C-methyl-cytidine, a potent inhibitor of Repatitie C virus replication)

817294-32-3 C88EGS 38.53

Cycidine, W-benzoy1-2:-deoxy-2:-fluoro-2:-methyl-, 3:,3:-dibenzoate, (2'R)~ (9CI) (CA IRDEX NAME)

Absolute stereochemistry. Rotation (+).

863329-65-1 CAPLUS 38

Gridise, 2'-decxy-2'-fiboro-2'-webbyl-, 3',5'-dibenzoate, (2'R)~ (901) (CA INDEX NEMB)  $\mathcal{L}(\mathcal{Q})$ 

Absolute storeochemistry. Botation (+).

817284-38-99

Rid SPN (Synthetic preparation); FREP (Preparation) (design, synthesis via fluorination, and antiviral activity of 2:-000xy-2:-fluoro-2:-C-methyl-cytidine, a potent inhibitor of Repatitis C virus replication)

8387

817204-38-3 CAPLUS Cytidine, 2'-deoxy-2'-fluoro-2'-wethyl-, monohydrochiomide, (2'8)- (901)  $\mathbb{C}\,\mathbb{G}$ (ĈA ISDEX NAMB)

absolute stereochewistry. Rotation (\*).

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ARSWER 10 OF 16 CAPTERS COTYPISST 2007 ACS OF STN 1.4

2005:34765 CAPLUS AR.

142:94074  $\mathbb{D}\mathbb{N}$ 

Proparation of modified finorinated (2'E)-2'-decxy-2'-finoro-2'-C-methyl  $\mathcal{H}_{\mathcal{X}}$ mucleoside analogs as antivital agents

115%

Clark, Jeremy Fracmasset, bid., Bachados PΑ

PCT Int. Appl., 228 pp.

CODER: PLXXDZ

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			GB,	GB,	ØK,	8B8.,	8335	30%	33.7	IN,	IS.	38%	BEC.	EG,	Хξ1,	NE,	×8,	SC.		
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			27.	80,	X2,	880,	2035	73.	TM.	$\mathcal{M}^{\mathfrak{P}}_{+}$	88.	80,	OM,	OY,	98,	DE,	D8,	388		
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                            32
                                  28939538
     WO 2004-0812472
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     MARPAY 142:94974
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The disclosed invention provides nucleoside analogs I, wherein B is puring and pyrimidine modleobase; X is O. S. CB2. Se. MM, M-alkyl, CBW, C(M)2; W is F, Cl. Br. iodo: Bl is B, phosphate, B-phosphoness, acyl, Sb, sikyl, cerboxyalkylamieo, eulfonate ester, peptide, amino acid, sugar reside; E2 and BE are independently B. alkyl, slkenyl, alkynyl, vunyl, GB. CN, helogen, MC2, ester, alkosy, thioalkyl, solfoxide, sulfoxyl; R6 is slkyl, CM, Me, OME, GB1, CB2OM, CM2W, B3, CBCM, CB2N3, CB2NB2, CB2NBMP, CB2NMP2, alkylne; and methods of treating a Flaviviridae infection, including bepatitis C virus, West Mile Virus, yellow fever virus, and a rhipovirus infaction in a host, including animals, and especially human, using a (2'R)-2'-decxy-2'-fluoro-2'-C-Me sucleosides, or a pharmaceutically acceptable salt or prodreg thereof. Thus, (2'R)-2'-deoxy-2'-fluoro-2'-Cmethyloytiding was prepared and tested as autiviral agent. The affects the nucleoside analogs tested on homan bone marrow cells are reported. (218)-21-deoxy-21-Elboco-21-C-methylcytidine shows activity against Bhinovirus, West Nile virus, 70110% Fever virus, and Deague virus. Cytotoxicity and effect of sucleoside analogs on human bone marrow cells are reported.

ET 817264-33-49

EL: PAC (Frankscological activity); aCT (Beactast); SPS (Systhetic preparation); TBS (Therapeutic use); SIGE (Biological study); FEEP (Freparation); EACT (Beactast or reagent); DEEE (Uses) (preparation of modified fluorisated (2'8;-2'-deoxy-2'-fluore-2'-0-me

-(preparation of modified linorinated  $(2/8) \times 2 \times deoxy \times 2 \times flhore \times 2 \times constant agents)$ 

PG 817284-33-4 CAPEGS

CM Cytidine, 2'-decxy-2'-finoro-2'-methyl-, (2'%)- (CA Immex Wame)

absolute stereochemistry. Botation (\*).

12 817294-38-92

NL: R&C (Pharmacological activity); BFM (Synthetic preparation); RBC (Therapeutic use); BIOL (Biological study); PREM (Preparation); USES (Uses)

(preparation of modified fluorinated (2°R)-2'-deoxy-2'-fluoro-2'-C-me nucleoside analogs as activiral agents)

RM 817204-38-9 CAPLUS

CR Cytidine, 2'-deczy-2'-flaczo-2'-methyi-, moschydrochloride, (2'R)- (9CE) (CA (BDEX MEMB)

absolute stereognemistry. Rotation (+).

🗱 же і

817204-44-7 830

RE: PAC (Fbarmacological activity); THO (Therapeutic use); MIOE

(Biological study); UBEB (Gses) pocleoside analogs as sutiviral agents)

817204-44-7 CAPLOS 8.8

Cyclidine 5'-(tetrahydroges triphosphate), 2'-deoxy-2'-flooro-2'-methyl-, (k/k)- (CA INDEX NAME)

Absolute stersochemistry.

817204-32-39 817204-37-89  $\mathfrak{XX}$ 

RE: RET (Reactant): SPE (Synthetic preparation); PEEP (Freparation); RACT (Reactant or reagent)

(preparation of modifies fluorinated (2-x)-2-deoxy-2-fluoro-2--0-80 nucleoside analogs as antiviral agents;

80 837204-52-3 CBFLUS

Cytidine, R-benzoyl-2'-deoxy-2'-fluoro-2'-metnyl-, 3',5'-dibenzoete, (2.8) - (901) (CA INDEX MANE)

Absolute stersochemistry. Botation (\*).

8)7294~37~8 CAPLES 8.83

Cycidine, W-benzogi-2'-deoxy-2'-fluoro-2'-methyl-, 3',8'-CMbistrifluorogoscare), (2.x)~ (9CI) (CA INDEX NAME)

Absolute Stereochemistry.

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